REMARKS

CLAIM REJECTIONS – 35 USC 112

The Examiner stated Claims 1 and 4-12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. According to the Examiner, the claims contain subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The Examiner continued as follows: The instant claims are generic with respect to "bioactive agent" and have not been sufficiently described to show possession of compositions comprising the entire genus. The invention defined by the claims requires a specific type physiochemical interaction between the bioactive agent and a polymer in order to produce the desired result.

The Examiner declared the showing in the specification, limited to ziprasidone, is not sufficient to show possession of all such materials in the context of the invention. The Examiner noted that applicant has amended the claim to add new limitation such as polyester carbonate, polyester carrying two or more carboxyl groups situated in medial portions off said polymer. But the Examiner stated that applicant has not provided the specific structural configuration of the polymers, in the absence of which, the structural and functional characteristics cannot be deduced.

Applicants respectfully traverse this written description rejection under 35 USC 112. First, applicants' claims are not, contrary to the Examiner's statement in the May 29, 2008 Office Action "generic with respect to 'bioactive agent'". Applicants' Claim 1 states that the bioactive agent is a *basic* bioactive agent. Secondly, Claim 1 indicates that said basic bioactive agent and the absorbable liquid polymer recited in the Claim are "at least 50 percent ionically bonded together". Accordingly, not just any bioactive agent is

recited. The bioactive agent is a) basic, and b) one which can be at least 50 percent ionically bonded to its corresponding absorbable liquid polymer.

That only ziprasidone is included in the specification does not mean that the claimed invention lacks written description. The requirement for written description is not a specification "to show possession of all such *materials* in the context of the invention" (emphasis added, but otherwise as stated by the Examiner in the May 29 Office Action). Rather, the written description requirement of 35 USC 112 exists to ensure that the inventors had within their possession at the time the application was filed a sufficient conception of the claimed invention such that they could describe their claimed invention in writing. In other words, it is not required to evidence possession of every embodiment, but rather sufficient possession of the claimed *invention* such that it could be described. In the instant case, applicants have in their specification provided adequate description of bioactive agent in the context of their invention. For example, starting on page 2, line 35, through page 3, line 21, a description of the term "bioactive agent" is provided. It is stated, for example, that "Bioactive agents contemplated for use in the invention can be natural or synthetic, acidic, or basic. Basic bioactive agents are preferred, including e.g. those that are amine-containing, i.e. those containing one or more amine groups. Other basic bioactive agents contemplated for use with the invention are basic drugs that are simple organic compounds having a molecular weight of more than 150 Da. The drug can also be a peptide comprising at least two amine-acid sequences, or it can be a protein."

The "bioactive agent "is further described in many other places in the specification, as is the absorbable liquid polymer. The interaction between the bioactive agent and the absorbable liquid polymer is also described in great detail in the specification. For example, on page 4, it is stated, "Representatively, the liquid conjugate of the invention may be made as follows: the solid bioactive agent is contacted with one or more liquid polymers described above under conditions effective to cause sufficient proton transfer whereby ionic conjugation between the basic aspects or moieties of sad drug (or said polymer as the case may be) and said acidic aspects or moieties of said polymer (or the drug as the case may be) occurs". From this, it is apparent that the

bioactive agent must have aspects or moieties that are capable of transferring protons to aspects or moieties of the polymer or vise versa.

Based on the above, applicants respectfully request that the written description rejection under 35 USC 112 of the Claims 1 and 4-12 should be withdrawn.

CLAIM REJECTIONS – 35 USC 103

The Examiner expressed that Claims 1 and 4-12 are rejected under 35 U.S.C. 103 as being unpatentable over Shalaby (U.S. Patent No. 5,714,159) in view of Kim et al. (U.S. Patent No. 6,232,304 B1).

The Examiner sated that, in Shalaby, the copolymer comprises a base component, designated as "Component A". According to the Examiner, "Component A" comprises a molecular chain having a hydrophilic block "Y" and a relatively hydrophobic polyester block "X". The hydrophobic block/segmented polymer comprises a polyester formed by grafting a glycolide, lactide, epsilon, caprolactone, p-dioxanone, trimethylene carbonate or combinations thereof, onto the hydroxylic or amino groups of the hydrophilic polymer precursor. The hydrophilic block comprises a polyoxyethylene, poly(oxyethylene-b-oxypropylene), polypeptide polyalkylene oxamate, a polysaccharide, and derivatives thereof; or a liquid, high molecular weight polyether glycol interlinked with an oxalate or succinate functionalities in linear or branched from (citing column 6 and 7, lines 65-67 and 1-15).

The Examiner stated that "Component A" optionally comprises carboxylic end groups which facilitates ionically binding a bioactive agent or drug (citing column 7, lines 19-23). The Examiner stated that the composition comprises an absorbable carrier which helps in immediate and controlled release of the bioactive drug (citing column 7, lines, 30-33).

According to the Examiner, Shalaby discloses that to render "Component A" more receptive to basic drugs, its end-groups can optionally be carboxylated (citing column 10,

lines 1-5). The Examiner stated that "Component A" can be succinylated to provide acidic end-groups for ionic binding on the bioactive agent/drug (citing column 12, lines 8-10).

The Examiner stated that although Shalaby does not specifically teach the bioactive agent such as ziprasidone, Kim et al. discloses that increasing drug solubility and stability of ziprasidone through appropriate formulation can lead to therapeutic efficacy of the drug (citing column 1, lines 17-20, of Kim et al.).

The Examiner concluded that in the instant case, due to the basic characteristics of ziprasidone and the claimed polymer, a skilled artisan would have expected to form ionic conjugated product with a reasonable expectation of success.

Applicants respectfully traverse this rejection. Applicants' claimed invention relates to a *liquid* conjugate comprising a basic bioactive agent and an absorbable liquid polymer (see pending Claim 1, emphasis added). The conjugates are useful in pharmaceutical formulations, for example injectable depot formulations (see page 5, lines 17-19, and page 5, line 36, through page 6, line 2, of Applicants' specification). The conjugates can assist in increasing the solubility of a drug compound (see for example page 2, lines 23-24, of the specification). Furthermore, in Claim 1 as now amended, the absorbable liquid polymer is selected from a polycarbonate, a polyester-carbonate and a polyester carrying two or more carboxyl groups situated in medial portions.

Shalaby (U.S. Patent 5,714,159, *supra*) provides a hydrogel-forming, self-solvating, absorbable polyester copolymer capable of selective, segmental association into a compliant hydrogel mass on contact with an aqueous environment (see Col. 6, lines 28-33, of Shalaby). Said copolymer comprises a "Component A" which is the basic structure of the Shalaby invention and which comprises as a hydrophobic block a polyester and as a hydrophilic block a polyoxyethylene, poly(oxyethylene-b-oxypropylene), polypeptide polyalkylene oxamate, a polysaccharide or a liquid high molecular weight poyether glycol interlinked with an oxalate or succinate funtionality.

Note thus that the basic structure, "Component A", of the polymers discussed in Shalaby do not essentially include terminal or otherwise accessible carboxyl moities.

It is noted that the Examiner has removed the rejection of anticipation over Shalaby. It is true that Shalaby does not disclose the specific polymers which are used to prepare the claimed conjugates.

Shalaby teaches hydrogel-forming copolymers which form a compliant hydrogel mass on contact with aquoeous environment. However, looking at the Examples provided in Applicants' specification, Applicants' claimed liquid conjugates do not gel and remain essentially liquid when contacted with an aqueous medium. In Example 7, on pages 12-13, of the Application, exemplary conjugates of the claimed invention are exposed to phosphate buffered saline (PBS). PBS is an aqueous medium. However, no hydrogel mass is formed when the exemplary conjugates are contacted with the PBS.

Thus, combining Shalaby with ziprasidone (disclosed in Kim et al.), as suggested by the Examiner, would not, contrary to the Examiner's assertion, arrive at Applicants' claimed invention.

Applicants submit that the Examiner is using hindsight reasoning. It is true that ziprasidone has basic moieties. But to conclude that it would have been obvious to use ziprasidone (due to its basic moities) in combination with the polymers described in the Shalaby reference to form the claimed liquid conjugates uses hindsight reasoning: First, their is no mention in the Shalaby reference to use basic drugs. There is no suggestion to form ionic interactions in the Shalaby reference. And there is no suggestion in the Shalaby reference to use the polymers therein to increase the solubility of a drug substance. It would not have been obvious to use ziprasidone with the polymers in the Shalaby reference. And, even if one did combine ziprasidone with the polymers in the Shalaby reference, there is no teaching in the Shalaby reference, or the Kim et al. reference, of which specific polymer type to use with ziprasidone and how to combine the two components (ziprasidone and absorbable liquid polymer) such that they result in a liquid conjugate comprised of at least 50 percent of the two components ionically bonded

together. Shalaby does not disclose the specific types of polymers that are encompassed by Applicants' claims. Thus, the Examiner is using hindsight reasoning to arrive at the claimed subject matter, a liquid conjugate comprising a basic bioactive agent and an absorbable liquid polymer selected form a polycarbonate, a polyester-carbonate and a polyester carrying two or mor carboxyl groups situation in medial portions off said polymers, wherein said basic bioactive agent and said absorbable liquid polymer in said liquid conjugate are at least 50 percent ionically bonded together.

If a telephone interview would be of assistance in advancing the prosecution of the subject application, the Examiner is invited to telephone the undersigned at the number provided.

No fee other than the fee for the three month extension of time authorized herewith is believed necessary in connection with this Communication. But if any other fee is determined necessary in connection with filing this Communication, such fee may be charged to Deposit Account No. 16-1445.

Respectfully submitted,

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